

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
16 June 2005 (16.06.2005)

PCT

(10) International Publication Number  
**WO 2005/054446 A3**

(51) International Patent Classification<sup>7</sup>: **C12N 5/06**,  
A61K 31/737, 47/36

August [BE/BE]; Zanddstraat 12, B-9810 Eke-Nazareth (BE). VEYS, Eric [BE/BE]; Klossesstraat 48, B-9052 Zwijnaarde (BE).

(21) International Application Number:  
PCT/BE2004/000171

(74) Agents: **BIRD, William, E.** et al.; Bird Goën & Co, Klein Delenstraat 42 A, B-3020 Winksele (BE).

(22) International Filing Date: 2 December 2004 (02.12.2004)

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/526,492 2 December 2003 (02.12.2003) US

(71) Applicant (*for all designated States except US*): **UNIVERSITEIT GENT** [BE/BE]; Sint-Pietersnieuwstraat 25, B-9000 Gent (BE).

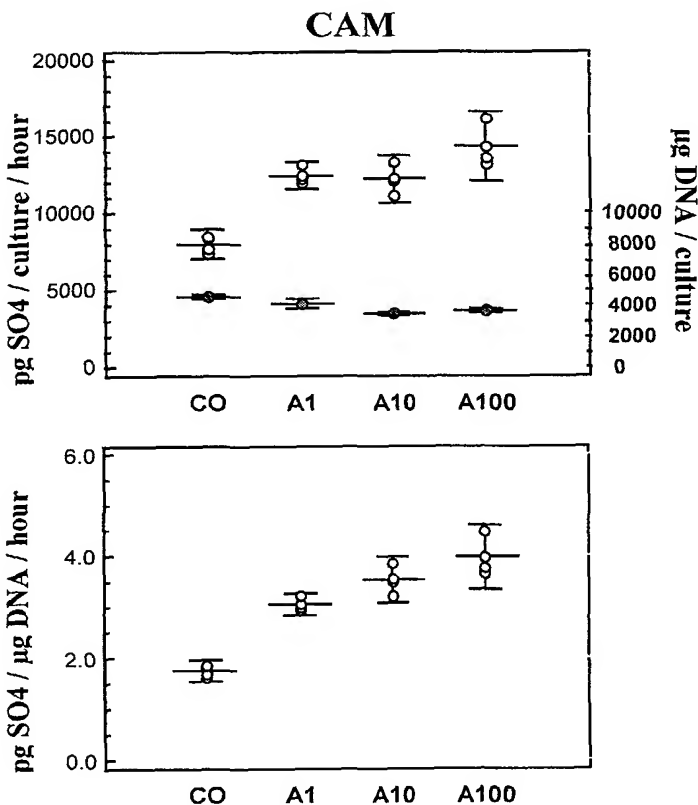
(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **VERBRUGGEN**,

[Continued on next page]

(54) Title: USE OF POLYSULPHATED ALGINATE IN CELLULAR MATRICES



(57) Abstract: The present invention describes an *in vitro/ex vivo* method for the cultivation of connective tissue cells or progenitor cells (e.g. chondrogenic cells) in matrix comprising polysulphated alginate. These cultivated cells can be used in the preparation of a medicament for the treatment or prevention of osteochondral defects. The invention also describes a matrix comprising polysulphated alginate and mammalian connective tissue cells or progenitor cells thereof.

WO 2005/054446 A3



European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

**Declaration under Rule 4.17:**

— *of inventorship (Rule 4.17(iv)) for US only*

**(88) Date of publication of the international search report:**

28 July 2005

**Published:**

— *with international search report*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/BE2004/000171

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C12N5/06 A61K31/737 A61K47/36

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, EMBASE, PAJ

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ALMQVIST K F ET AL: "Culture of chondrocytes in alginate surrounded by fibrin gel: Characteristics of the cells over a period of eight weeks" ANNALS OF THE RHEUMATIC DISEASES, vol. 60, no. 8, August 2001 (2001-08), pages 781-790, XP002331237 ISSN: 0003-4967 page 781, line 1 - page 785, left-hand column, paragraph 3	1-22
A	EP 1 027 893 A (GLIATECH INC; GLIATECH, INC) 16 August 2000 (2000-08-16) page 5, line 34 - page 6, line 20	1-22
A	US 2003/109493 A1 (VEYS ERIC MAXIMILIEN ET AL) 12 June 2003 (2003-06-12) page 2; example 1	1-22
	-/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

10 June 2005

Date of mailing of the international search report

27/06/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Heiduschat, C

# INTERNATIONAL SEARCH REPORT

Inter	al Application No
PCT/BE2004/000171	

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>VERBRUGGEN G ET AL: "Influence of polysulfated polysaccharides on aggrecans synthesized by differentiated human articular chondrocytes."</p> <p>THE JOURNAL OF RHEUMATOLOGY. AUG 1999, vol. 26, no. 8, August 1999 (1999-08), pages 1663-1671, XP009048846</p> <p>ISSN: 0315-162X</p> <p>cited in the application</p> <p>page 1670, left-hand column, paragraph 2</p>	1-22
A	<p>WO 98/11141 A (JOHNSON &amp; JOHNSON MEDICAL, INC; GRADY, MICHAEL, WILLIAM; DOYLE, PETER,) 19 March 1998 (1998-03-19)</p> <p>page 5 - page 13; figure 2</p>	1-22
A	<p>SCHWEIGER R G ET AL: "POLYSACCHARIDE SULFATES. II. SULFURIC ACID ESTERS OF GLYCURONANS HAVING VARIOUS DEGREES OF SUBSTITUTION"</p> <p>CARBOHYDRATE RESEARCH, AMSTERDAM, NL, vol. 21, 1972, pages 275-281, XP002049669</p> <p>page 275, line 1 - page 278, paragraph 5</p>	1-22

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/BE2004/000171

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1027893	A	16-08-2000	US 5605938 A	25-02-1997
			EP 1027893 A2	16-08-2000
			EP 1038528 A1	27-09-2000
			GR 2001300031 T1	29-06-2001
			GR 2001300032 T1	29-06-2001
			AT 197673 T	15-12-2000
			AU 671256 B2	22-08-1996
			AU 2146992 A	08-01-1993
			BG 98333 A	15-11-1994
			BR 9206077 A	15-11-1994
			CA 2110291 A1	10-12-1992
			CZ 9302594 A3	16-11-1994
			DE 1027893 T1	20-09-2001
			DE 1038528 T1	20-09-2001
			DE 69231574 D1	28-12-2000
			DE 69231574 T2	31-05-2001
			DK 586535 T3	05-03-2001
			EP 0586535 A1	16-03-1994
			ES 2156839 T1	01-08-2001
			ES 2156840 T1	01-08-2001
			ES 2151887 T3	16-01-2001
			FI 935345 A	13-01-1994
			GR 3034760 T3	28-02-2001
			HU 66427 A2	28-11-1994
			JP 3379757 B2	24-02-2003
			JP 6508356 T	22-09-1994
			JP 2000312715 A	14-11-2000
			JP 2002154973 A	28-05-2002
			JP 2002154972 A	28-05-2002
			JP 2002138039 A	14-05-2002
			JP 2002138040 A	14-05-2002
			KR 237731 B1	01-02-2000
			NO 934319 A	11-01-1994
			SK 134393 A3	10-08-1994
			WO 9221354 A1	10-12-1992
			US 2003069205 A1	10-04-2003
			US 5705177 A	06-01-1998
			US 5705178 A	06-01-1998
			US 6127348 A	03-10-2000
			US 6020326 A	01-02-2000
			US 5994325 A	30-11-1999
			US 6083930 A	04-07-2000
			US 6417173 B1	09-07-2002
US 2003109493	A1	12-06-2003	FR 2811572 A1	18-01-2002
			AU 7643701 A	30-01-2002
			CA 2416369 A1	24-01-2002
			EP 1301192 A1	16-04-2003
			WO 0205826 A1	24-01-2002
			JP 2004503594 T	05-02-2004
WO 9811141	A	19-03-1998	GB 2317182 A	18-03-1998
			AU 726555 B2	09-11-2000
			AU 4131597 A	02-04-1998
			BR 9711747 A	24-08-1999
			CA 2265780 A1	19-03-1998
			DE 69702862 D1	21-09-2000
			DE 69702862 T2	22-02-2001

# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/BE2004/000171

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9811141	A	DK 925310 T3	20-11-2000
		EP 0925310 A1	30-06-1999
		ES 2152107 T3	16-01-2001
		WO 9811141 A1	19-03-1998
		JP 2001500184 T	09-01-2001
		KR 2000036061 A	26-06-2000
		NO 991160 A	10-05-1999
		PT 925310 T	30-11-2000
<hr/>			